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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,842	02/10/2006	Nicolae Manolescu	P02250	7147

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
10/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO@hershkovitz.net
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Office Action Summary	Application No.	Applicant(s)	
	10/567,842	MANOLESCU ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3 and 4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/24/06,7/31/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities: [0012] recites, “the invention fathered by Mr. Gabor Somlayi are not convincingly because” which is not proper English. Appropriate correction is required.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what type of examination is being used as the instant claims merely recite, “the tumor nodules measurement and examination is performed on each 2-3 days”.

5. Claim 3 recites the limitation "the tumor cells" in step B). There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Somlyai et al. (US 5,855,921) and/or Somlyai et al. (*FEBS* **1993**, *317*, 1-4) in view of Bild et al. (Research concerning the radioprotective and immunostimulating effects of deuterium-depleted water, *Rom. J. Physiol.*, **1999** Jul-Dec, *36*(3-4), 205-18) and in further view of Rotinberg et al. (*Rom. J. Physiol.* **2000**, *37*, 91-103).

8. Somlyai et al. (US 5,855,921) discloses pharmaceutical products for curing tumorous diseases (i.e. breast cancer, prostate cancer, a sarcoma, a lymphoma, epithelioma, etc.) where the product comprises water with a deuterium content of 0.1 to 110 ppm and/or aqueous solutions suitable for human consumption (abstract; column 1, lines 5-13; column 3, lines 14-24 and 46-54; claim 9). The therapeutical application of the products of deuterium-depleted water containing deuterium from 0.1 to 100 ppm causes a decrease in the deuterium level of the organism and therefore the growth rate of the tumorous cells slows, the cell walls decay, while the healthy cells are still capable of tolerating decreasing deuterium concentration (column 3, lines 46-54). An in vivo experiment was used to investigate how the growth of tumors was influenced by decreasing the deuterium content in the drinking water of mice

transplanted with human breast tumors (column 4, lines 54+; table 1; column 5, lines 1-26). The animals of the control group consumed normal water, while from the day following the transplantation the animals belonging to the treated groups were supplied with D-depleted water prepared according to the invention (column 4, lines 54-64). Also, tumorous human prostatic cells and tumorous human colon cells were transplanted into CBA/Ca mice and the mice fed with water containing 94±5 ppm of deuterium drinking water (column 5, lines 27-41). The effect of deuterium-depleted water was examined for 88,90, etc. days (tables 2-4).

9. Somlyai et al. (*FEBS* **1993**, *317*, 1-4) discloses the use of deuterium-depleted water (30-40 ppm D) for the inhibition of tumor growth in xenotransplanted mice (abstract). For in vitro studies, L_{929} cells were allowed to grow till confluence and were treated with trypsin (to determine viability) and then the cells were treated with deuterium-depleted water. The effect on D concentration of the medium on the growth of L_{929} fibroblast cells by comparing the growth rates in DMEM prepared with deuterium-depleted water and normal water (p1, **2. Materials and Methods**; p2, **3.1 Effect of D on the growth rate of animal cell lines in vitro**). For in vivo studies, two different human breast adenocarcinoma were implanted subcutaneously in each flank of female CBA/Ca mice (p2, **2. Materials and Methods** continued). The drinking water of the mice in the treated group was replaced with deuterium-depleted water (30 ppm) one day after transplantation and the differences in the treated and control groups (normal water) examined over about 87 days (table II). On the 65th day, 72% of the tumorous mice in the control groups had already died but only 12% of the

animals in the treated groups had died (p2 and p3, **3.2 Effect of D concentration on tumor formation in mice**).

10. The references of Somlyai et al. do not disclose pretreating the mice with deuterium-depleted water and does not specifically disclose 60 ppm of deuterium-depleted water. Also, the references of Somlyai et al. do not disclose the use of Wistar outbred rats.

11. Bild et al. (*Rom. J. Physiol.*, **1999** Jul-Dec, *36*(3-4), 205-18) discloses that mice fed for 15 days with Deuterium-Depleted Water (30 ppm deuterium) had a statistically significant increased survival rate compared with control groups fed with normal distilled water (150 ppm deuterium), after 8.5 Gy irradiation (61% survival in the test group versus 25% in the control group). The hematological picture showed that normal WBC, RBC and platelet counts were maintained in the test groups. Immunological parameters (serum opsonic and bactericidal capacity, bactericidal capacity of the peritoneal macrophages) showed a marked increase in the test groups compared to a severe decrease in the control groups. Auxiliary tests using chemical radiomimetics (hydrochloric embihine) and immunosuppressors (cyclophosphamide) showed a strong protective effect of deuterium-depleted water against the decrease of the leukocyte counts and other immunologic parameters. In conditions of experimental inflammation induced with subcutaneous-implanted pellets, deuterium-depleted water feeding resulted in a statistically significant increase of the inflammatory response, demonstrated by increased percentages of PMN and lymphocytes in the peripheral blood and the increased phagocytic capacity of the peripheral blood PMN. All results show

a marked intensification of the immune defenses and increased proliferation of the peripheral blood cells, probably accounting for the radioprotective effects.

12. At the time of the invention it would have been obvious to one ordinarily skilled in the art to pretreat the mice, to be transplanted with tumors, with a deuterium-depleted water to allow for resistance to the cancer and thus examine the preventative characteristics of deuterium-depleted water toward tumor growth. It would also have been obvious to apply trypsin to the tumor cells to be transplanted into mice, as taught by Somlyai et al. (*FEBS* **1993**, *317*, 1-4), to test for their viability prior to transplantation.

13. The step of monitoring the animals physiological condition, food and water consumption and notifying the toxic condition occurrence of the instant claims is obvious as the mice were monitored over 87,88,90 days and thus it would have been necessary to provide adequate food and water to the mice and watch for toxic condition occurrences (i.e. death). The number of toxic condition occurrences (i.e. deaths) were listed in the tables 2-4 of Somlyai et al. (US 5,855,921) and table II of Somlyai et al. (*FEBS* **1993**, *317*, 1-4).

14. Somlyai et al. (US 5,855,921) teaches of the examination of the reduction of the growth rate of tumorous cells via the therapeutical application of the products of deuterium-depleted water containing deuterium from 0.1 to 100 ppm. Therefore, at the time of the invention it would have been obvious to one ordinarily skilled in the art to examine the concentrations of deuterium-depleted water necessary to cause the reduction of the growth rate of tumorous cells, such as 60 ppm. Also, the step of determining that the 60 ppm deuterium depleted

water as the concentration that is most efficient for cancer therapy is a mental step and does not require any actual manual steps.

15. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute or utilize Wistar outbred rats in place of the rats of the disclosures as Wistar outbred rats are the most popular rats used experimentally as evidenced by wikipedia (see laboratory rat).

16. The references of Somlyai et al. do not disclose 256 Walker sarcoma and T8 Guerin lymphotropic epitelioma.

17. Rotinberg et al. (*Rom. J. Physiol.* **2000**, *37*, 91-103) discloses the transplantation of 256 Walker sarcoma and T8 Guerin lymphotropic epitelioma into Wistar, white female rats for in vivo testing (p3, last paragraph and p4, paragraph 2).

18. At the time of the invention it would have been obvious to one ordinarily skilled in the art to substitute the known 256 Walker sarcoma and T8 Guerin lymphotropic epitelioma of Rotinberg et al. for the sarcomas and epitheliomas of Somlyai et al. as it is obvious to those skilled in the art to make known substitutions on compounds that are similar in structure and function to observe the effects on the function of such compounds and to use the observations/data to further manipulate a compound to generate the desired effect. Also, Rotinberg et al. clearly shows that the 256 Walker sarcoma and T8 Guerin lymphotropic epitelioma may be jointly transplanted into Wistar rats.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618